

## IMMUNIZATIONS IN THE ELDERLY\*

DAVID W. BENTLEY, M.D.

Monroe Community Hospital  
University of Rochester School of Medicine and Dentistry  
Rochester, New York

THE “modern” concept of immunization for older persons in the United States is at least 25 years old, beginning with recommendations for influenza vaccine. Recently, however, there is renewed interest in this and other vaccines for this high-risk group. This interest has developed because of the growing numbers of older people (currently approximately 29 million people 65 years of age and older with projections to approximately 35 million in the year 2000), their increased risk for complications and death following tetanus and influenza virus infections that can be effectively reduced by immunization, and the unexpected underutilization of the more recently licensed pneumococcal vaccine.

This review will focus primarily on the major vaccines that all older people should receive: tetanus-diphtheria toxoid, influenza virus vaccines, and pneumococcal vaccines. But one should not forget the select few other immunobiologics recommended in special circumstances that place any persons into a special high-risk group. These include: *special occupations*, (hepatitis B, polio, rabies, and plague vaccines); *lifestyles* (hepatitis B vaccine); *environmental situations* (hepatitis B vaccine), and *travel* to certain parts of the world where vaccine-preventable diseases are epidemic, endemic, or enzootic (polio, yellow fever, hepatitis B, rabies, meningococcal, typhoid, cholera, and plague vaccines and immunoglobulins). For further details see the recommendations of the Committee on Immunization,<sup>1</sup> Immunization Practices Advisory Committee for Adult Immunization,<sup>2</sup> and this Committee’s most recent recommendations on the specific immunobiologics, published in the *Morbidity and Mortality Weekly Report*.

### TETANUS-DIPHTHERIA TOXOID

*Justification for use in older people.* Although the number of cases in the United States is low (approximately 100 per year) compared to developing

\*Presented as part of the Fourth Annual SK & F/FSK Anti-Infective Conference, *Controversies in Diagnosis and Management of Infectious Disease*, held by the Division of Infectious Diseases/Epidemiology of the College of Physicians and Surgeons of Columbia University and funded by a grant from Smith-Kline French Laboratories/Fujisawasa-Smith-Kline at Orlando, FL, September 7-9, 1986.

countries, tetanus continues to cause serious health problems for older people. The average annual incidence rate for 1982-1984 was 0.036/100,000 total population but the age-specific incidence rates for those 60 years of age and older was 0.132/100,000.<sup>3</sup> This high-risk group accounted for approximately 60% of the reported cases, with a case-fatality rate of approximately 60%. Of the 253 cases, approximately 70% of the cases occurred after an identified acute injury; approximately one half, however, were related to lacerations (versus puncture wounds) and approximately 40% of the acute wounds occurred indoors. In addition, approximately 20% of the cases were associated with chronic wounds or underlying medical conditions such as skin ulcers, abscesses, or gangrene.<sup>3</sup>

There is no natural immunity to the toxin (tetanospasm) of *Cl. tetani*, thus tetanus occurs almost exclusively in those who are unimmunized, inadequately immunized, or whose history of immunization is unknown.<sup>3</sup> Protective serum antitoxin levels ( $\geq 0.01$  units/ml) are present in 35% to 55% of community-residing older persons.<sup>4,5</sup> The prevalence of protective titers in elderly nursing home residents/patients ranges from 30% to 50%.<sup>4,6</sup> In both settings a lower proportion of women are protected. This is not age-dependent, and appears to be correlated with contact with organized military medical care beginning in the early 1940s.<sup>4,6</sup> A history of fewer than two doses of toxoid correlates well with nonprotective titers<sup>5</sup> and the occurrence of disease.<sup>3</sup>

Although a similar low prevalence of diphtheria protective antitoxin antibody levels can be demonstrated in older people,<sup>4,6</sup> diphtheria is not as serious a problem for the elderly as is tetanus.<sup>7</sup>

*Immunizing agent.* The current recommended immunizing agent for older persons is tetanus-diphtheria toxoid adsorbed for adult use, which is a combined preparation recommended for all people more than seven years of age.<sup>7</sup> Tetanus-diphtheria toxoid is an effective immunizing agent for older persons. Protective tetanus antitoxin antibody levels following immunization occur in approximately 40% of nonimmune older subjects after the first dose, approximately 85% following a second dose and in 100% after the third dose.<sup>8</sup> The duration of protective levels is somewhat reduced in older patients, and approximately 25% of those immunized eight years previously have antitoxin serum levels of  $\leq 0.01$  units/ml. But approximately 93% of these respond to a booster immunization with protective antibody levels.<sup>9</sup>

Information on adverse reactions following tetanus-diphtheria toxoid in older people is scant, but the risk is probably considerably less than the overall rates, i.e., approximately 33 reported clinical illnesses (within 30 days

of immunization) per million doses administered for all subjects.<sup>10</sup> The only contraindication to this toxoid is a history of neurological (febrile or non-febrile convulsions, encephalopathy or focal neurologic signs) or severe hypersensitivity reaction associated with a previous dose.

*Current recommendations.* Immunization is recommended for all older people who are unimmunized, inadequately immunized, or whose history of immunization is unknown. The routine immunizing schedule for older subjects requires a series of three doses (called primary immunization) and is identical to that recommended for all adults.<sup>7</sup> The booster immunization is administered every 10 years after the last dose, provided the primary series has been completed. Guidelines for tetanus prophylaxis in the management of wounds has been further simplified.<sup>7</sup> If the history of tetanus toxoid immunization is unknown or less than three doses, tetanus-diphtheria toxoid is recommended following all wounds. It is recommended for clean and minor wounds if the third dose was more than 10 years earlier and for all other wounds if the third dose was more than five years earlier.

#### INFLUENZA VACCINES

*Justification for vaccine use.* Influenza virus infection is an important communicable disease for older patients, especially those with chronic cardiac and respiratory conditions. Although people 65 years of age and older comprise only approximately 13% of the total American population and their rates of infection with influenza virus are relatively low (10%), they account for at least 50% of the hospitalizations and 75% to 80% of the deaths attributed to influenza.<sup>11</sup> Excess hospitalization rates during influenza A epidemics for those 65 years of age and older vary substantially with the presence of high-risk conditions: from 150 to 172/100,000 among those without underlying high-risk conditions to 476 to 636/100,000 with underlying high-risk conditions.<sup>12</sup> The estimated rates of influenza-associated mortality during influenza A epidemics among patients 65 years of age and older range from 9/100,000 among those with no high-risk conditions to 217/100,000 among those with one high-risk condition to 306/100,000 among those with two or more high-risk conditions. The highest estimated rates are among patients with underlying cardiovascular disease combined with either diabetes or chronic pulmonary disease.

Prevention of influenza virus infection by immunization is a formidable task. Influenza A viruses, the primary cause of severe illness, are classified into subtypes on the basis of their haemagglutinin (H) and neuraminidase (N) antigens. Sufficient antigen variation or drift within the same subtype,

e.g., A/Texas/77 (H3N2) and A/Bangkok/79 (H3N2), may occur over time so that infection or immunization with one strain may not induce immunity to distantly related strains. Major antigenic shifts, which herald pandemic influenza, produce “new” viruses to which the population has no immunity, e.g., the shift in 1957 from H1N1 to H2N2. Influenza B viruses also cause disease in older people and, although they are much more antigenically stable than influenza A viruses, antigen variation does occur. Consequently, influenza vaccine must be administered each year and must include inactivated expected virus strains.<sup>13</sup>

*Immunizing agent.* Inactivated influenza virus vaccines have been the principal means for preventing influenza since the late 1940s. In general, the vaccine has contained both A and B type virus, usually the types isolated in the previous winter’s influenza season. Recent influenza vaccines have consisted of an inactivated trivalent preparation containing H1N1 and H3N2 influenza A antigens and an influenza B antigen. For the 1986-87 season, the preparation contains 15 $\mu$ g each of A/Chili/1/83(H1N1), A/Mississippi/1/85(H3N2) and B/Ann Arbor/1/86 hemagglutinin antigens in each 0.5 ml. One dose intramuscularly in the deltoid muscle is required for older persons.<sup>13</sup> For this season an additional monovalent influenza A (H1N1) vaccine is recommended for protection against a newly emerged variant of influenza [A/Taiwan/1/86(H1N1)] causing outbreaks among children and young adults in Asia.<sup>14</sup>

Acute local reactions with mild to moderate soreness around the vaccination site occur in approximately one third of vaccinees and persist one to two days. Systemic reactions, including fever with or without a flu-like illness, occur in <1%, begin 6 to 12 hours following vaccination, persists for one to two days, and appear to be less severe in older persons.<sup>15</sup> Contraindications to vaccination include a previous history of Guillain-Barre Syndrome or anaphylactic hypersensitivity to eggs.<sup>13</sup>

Neutralizing, hemagglutination-inhibiting (HAI) and complement-fixing (CF) are predominantly IgG antibodies that develop in the serum of patients with primary infection beginning in the second week after exposure to the antigen and peak by four weeks.<sup>15</sup> Although there is no exact correlation, protection against influenza is generally due to adequate titers of antibody directed against the H antigen, i.e., serum HAI antibody titers of 1:40 or greater.<sup>16</sup> Secretory antibodies also develop in upper respiratory tract secretions, but are quantitatively directly related to serum antibodies. Antibody

responses following immunization resemble those following natural infection, including the presence of detectable secretory antibody in respiratory secretions.

In general, serum antibody responses to vaccination in older subjects are comparable to young healthy adults. The proportion of elderly vaccinees who develop serum HAI antibody titers of  $\geq 1:40$  postvaccination are 46% to 100% for H3N2 vaccine antigens, 40% to 92% for H1N1 antigens and 20% to 69% for B antigens.<sup>17</sup> Similar recent studies in nursing homes indicate that 39% to 64% and 17% to 63% of institutionalized older patients develop HAI antibody titers of  $\geq 1:40$  postvaccination to H3N2 and B antigens, respectively.<sup>18</sup> These responses are significantly lower than among young healthy adults, and suggest that older people with chronic diseases, medications, or other conditions associated with institutionalization may be expected to respond less satisfactorily to inactivated influenza vaccines. The nasal secretory antibody response in older patients following influenza vaccination appears comparable to young healthy adults.<sup>19</sup>

When influenza vaccine antigens are closely matched with the epidemic strain and studied in placebo-controlled trials, the efficacy rate for reducing influenza infection among young healthy adults ranges from 67% to 92%.<sup>15</sup> In a placebo-controlled trial among healthy older people, the efficacy rate was 96%.<sup>20</sup> A retrospective study demonstrated that influenza vaccine reduced pneumonia and influenza-associated hospitalizations and deaths among community-residing older persons by 72% and 81%, respectively.<sup>21</sup> A recent uncontrolled prospective study of outbreaks in nursing homes indicated that the efficacy of influenza vaccine in uncomplicated illness was relatively low, (28% to 37%) but that its efficacy in reducing complications, including hospitalization (47%), pneumonia (58%), and death (76%) was unusually high.<sup>22</sup>

*Current recommendations.* The current recommendations for the 1986-87 influenza season consist of a standard trivalent vaccine and the use of amantadine for the prevention and treatment of influenza A virus infections.<sup>13</sup> Supplemental monovalent influenza A (H1N1) vaccine is recommended for those 35 years of age or younger with high-risk chronic disorders (see below), because those born before the mid 1950s were exposed to this virus frequently from the mid 1930s onward from sporadic outbreaks and worldwide epidemics and, as a result, have developed a moderate degree of immunity to A/H1N1 strains. Outbreaks of influenza A (H1N1) infection in high-

risk nursing home patients, however, do occur,<sup>23</sup> which suggests that scattered outbreaks in this high-risk group with the current A/Taiwan/1/86(H1N1) strain may be anticipated.

The elderly (age 65 years or older) subgroups for which active targeted vaccination efforts have the highest priority include: those persons with chronic disorders of the cardiovascular or pulmonary systems severe enough to have required regular medical follow-ups or hospitalization during the preceding year and residents of nursing homes and other long-term care facilities. With a slightly lower priority, the vaccine should also be readily available to older people at moderate medical risk of influenza-related complications with the general population. These include: those with chronic metabolic diseases, including diabetes mellitus, renal dysfunction, anemia, immunosuppression, or asthma severe enough to have required regular medical follow-ups or hospitalization during the previous year, and those otherwise healthy. In addition, physicians, nurses, and other health-care team personnel, as well as providers of care in home settings, should also receive influenza vaccination annually if they have extensive contact with these high-risk older patients.<sup>13</sup>

#### PNEUMOCOCCAL VACCINE

*Justification for vaccine use.* Pneumococcal disease remains an important cause of morbidity and mortality for older persons. The incidence of pneumococcal infections is estimated at 21 to 43/100,000 per year<sup>24</sup> and increases for older people to 125 to 245/100,000 per year.<sup>25</sup> The overall bacteremia rate is approximately eight cases per 100,000; the rate for older patients is more than two times this rate.<sup>24,26</sup> Pneumococcal pneumonia among older people is substantially more frequent than the overall incidence of pneumococcal pneumonia, which is in the range of 1 to 2/100,000 per annum.<sup>27</sup> The estimated incidence of pneumococcal pneumonia in community-residing older persons is approximately 3/100,000 per annum<sup>28</sup> and 13 to 16/100,000 per annum for the institutionalized elderly.<sup>29</sup> In addition, case-fatality rates, as high as 40% for bacteremia and 55% for meningitis,<sup>30</sup> occur in older patients despite the availability of such potent antimicrobials as penicillin. Moreover, even when penicillin is used in the first day or two of illness, there is a limited effect on the outcome of the disease among those "destined" to die within the first five days of illness.<sup>31</sup>

*Immunizing agent.* The currently recommended immunizing agent is pneumococcal vaccine, polyvalent. The vaccine was licensed in the United States

in November 1977, and contained purified capsular polysaccharides from 14 of the 83 different types of *S. pneumoniae*. In July 1983 an expanded 23-type vaccine was licensed containing purified polysaccharides from serotypes: 1-5, 6B, 7F, 8, 9N, 9B, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, and 33F (Danish nomenclature). The new vaccine is so formulated that each 0.5 ml dose contains 25  $\mu$ g per component in a diluent of isotonic saline containing 0.25% phenol (PNEUMOVAX) or 0.01% thimerosal, a mercury derivative (PNU-IMUNE), as preservative. The dose is administered subcutaneously or intramuscularly. Pneumococcal vaccine and influenza vaccine can be given at the same time if different sites are used; without decreasing the antibody response of either vaccine or substantially increasing the side effects.<sup>30</sup>

Vaccine-associated reactions occur within 24 hours of injection in 10 to 15% of elderly vaccinees, and consists primarily of discomfort, erythema and induration which lasts 5-10 days (mean 1.7 days). Fever, 100°F or greater, occurs in approximately 2% and generally lasts less than 24 hours.<sup>28</sup> Severe local and systemic reactions with fever (>103°F) headache, myalgias, and chills have been reported, usually in younger adults and those revaccinated.<sup>32</sup> These reactions occur two to eight hours following the injection, and probably represent an arthus-type hypersensitivity reaction. Acute anaphylactoid reactions are rare, occurring in approximately five per million doses administered.<sup>30</sup> The only contraindication to the vaccine is a history of allergy to one of the vaccine components, usually the diluent.

The mechanism of protection following vaccination is similar to natural infection and depends on the production of opsonizing antibodies that promote phagocytosis of the homologous types. The level of type-specific antibody which is protective against each type has not been determined, but appears to be >200-300ng Ab N/ml.<sup>33</sup> Most adults respond to the vaccine in two weeks with a maximum response in approximately four to six weeks. Antibody to serotypes of *S. pneumoniae* represented in the vaccine persist at 30% to 50% of peak levels among healthy, middle-aged people for at least five to six years.<sup>34</sup>

Some studies suggest that the immune response to the vaccine in older people is satisfactory.<sup>35,36</sup> A preliminary study of the 14-valent pneumococcal vaccine in a small group of institutionalized older patients, however, demonstrated significantly lower antibody responses at 1- and 12 months postvaccination and significantly fewer elderly subjects with "protective" antibody levels, i.e., >300ng Ab N/ml at 12 months following vaccination than

among young healthy adults.<sup>17</sup> This suggests that, although some responded as well as younger subjects, institutionalized elderly patients, especially those more than 80 years of age, may not be as well protected by pneumococcal vaccine as previously considered. The duration of protective levels of antibody in the elderly following vaccination is unknown.

Randomized controlled efficacy trials of pneumococcal vaccine in older adults have demonstrated less than satisfactory results.<sup>37</sup> Studies based on comparing distributions of serotypes of *S. pneumoniae* isolated from vaccinated and unvaccinated subjects, however, demonstrate an estimated efficacy of approximately 60% for persons more than 65 years of age with or without chronic underlying diseases.<sup>38</sup> Similar results were noted for all those more than 55 years of age in recent efficacy studies using a case-control approach.<sup>39</sup> Other studies, although uncontrolled, suggest that vaccination may be less effective among the institutionalized elderly.<sup>40</sup>

*Current recommendations.* The most recent recommendations from the Centers for Disease Control for older persons are as follows:<sup>30</sup> Those with chronic illnesses, especially cardiovascular disease and chronic pulmonary disease, who sustain increased morbidity with respiratory infections; those with chronic illnesses specifically associated with an increased risk for pneumococcal disease or its complications, e.g., those with splenic dysfunction or anatomic asplenia, Hodgkin's disease, multiple myeloma, cirrhosis, alcoholism, renal failure, cerebrospinal fluid leaks and conditions associated with immunosuppression; those aged 65 and older who are otherwise healthy; and those undergoing elective splenectomy or immunosuppressive treatment, as in patients who are candidates for organ transplants, should be vaccinated at least two weeks, or as long as possible, prior to the treatment.

Because of an increase in adverse reactions among adults that appears to correlate with elevated antibody levels (40), and because additional doses of pneumococcal vaccine provide a poor "booster" response, the vaccine should be given only once to adults. Older patients who have received the 14-valent pneumococcal vaccine should not be revaccinated with the 23-valent vaccine because the modest increase in coverage of added types does not warrant the possibly increased risk of adverse reactions.

#### COST-EFFECTIVENESS OF THE RECOMMENDED VACCINES

To evaluate the benefits of the vaccines targeted for older patients, from the point of view of the population as a whole or for certain groups in the population, two related techniques, cost-effectiveness analysis and cost-benefit analysis, are used.<sup>43</sup> Both techniques aggregate the net medical care costs



TABLE I. COST-EFFECTIVENESS MODEL FOR VACCINATION<sup>47,48</sup>

Net medical costs = $C = (C_p - C_t + C_{se} - C_i)$
Net health effects = $E = (E_{ly} + E_m - E_{se} - E_i)$
$C_p$ = + cost of vaccination
$C_t$ = - costs of treating prevented disease
$C_{se}$ = + costs of treating vaccine side effects
$C_i$ = + costs of treating other illnesses in extended life
$E_{ly}$ = + years of life from prevented mortality
$E_m$ = + quality of life from prevented morbidity
$E_{se}$ = - morbidity from vaccine side effects
$E_i$ = - morbidity from future illness in extended life

and the net health benefits from a vaccination program versus the costs that would occur if there were no vaccination program and one relied exclusively on treatment of the disease should it occur. The major disadvantage of the cost-benefit analysis is that a dollar value is required on such difficult to measure benefits as the saving of a life or an increase in quality of life. For this reason, the cost-effectiveness analysis is generally preferred in calculating the changes in medical care costs and health effects from vaccination programs. The cost-effectiveness ratio (Table I) expresses the net medical costs that would be expended with vaccination to gain one year of healthy life for a vaccinated person. Here costs are limited to expenditures and savings within the medical-care sector. Net effects on health are expressed in quality-adjusted life years.

*Tetanus-diphtheria toxoid.* There has been little discussion of the cost-effectiveness of tetanus-diphtheria toxoid, probably because the incidence of tetanus, although relatively higher in older people, is still quite low (0.13/100,000 persons) compared to other vaccine preventable infectious diseases. Moreover, tetanus is not a contagious disease. Thus, the cost of the disease burden for society is quite low, although the cost to the individual older person may be as high as \$50,000 for treatment and recovery from tetanus.

The question of the desirability of large-scale immunization programs for older patients in nursing homes has been debated. Based on information from the Centers for Disease Control, there would be, at the most, two cases of tetanus in the 2.2 million older persons who occupy the 1.2 million nursing beds each year in the United States.<sup>43</sup> Unfortunately, there is no specific information about the incidence of tetanus in nursing home residents and patients in the United States, and attempts to estimate the occurrence of this disease in nursing homes by extrapolation from incidence data for

the total population is probably inappropriate.<sup>44</sup> Nevertheless, the total costs for the 2.2 million patients in nursing homes, at a minimal charge of \$5.00 for a single tetanus booster, would amount to 11 million dollars for this population. If only two deaths occurred due to tetanus per year, and if the life expectancy were estimated at five years (with an average age of 82.5), then a saving of 10 years might be expected, which would amount to more than a million dollars per life year saved.<sup>45</sup> This is clearly at the high (unfavorable) side of the cost-effectiveness ratio (Table II). Others have argued that, although it may not be cost-effective in the usual sense, the increased frequency and severity of tetanus in older persons, the likelihood of high-risk conditions afflicting the institutionalized elderly (cutaneous ulcers and peripheral gangrene) and the fact that tetanus-diphtheria toxoid is inexpensive, safe, and highly effective, support the concern that selected nursing home residents should receive immunization.<sup>17</sup>

*Influenza vaccines.* A cost-effectiveness analysis was performed by the Office of Technology Assessment of the U.S. Congress to evaluate influenza vaccination.<sup>46</sup> From 1971-72 through 1977-78 vaccination of an older person saved medical care costs while improving health. Even if survivors' medical costs were included, the cost per year of healthy life gained by vaccination was fairly low: \$1,782 for an average person age 65 years or older and \$4,040 for an elderly high-risk patient. Based on reported annual vaccination rates averaging 22%, annual influenza vaccination for these seven years for older people saved about 6.6 million dollars in net medical costs associated with epidemic influenza. If the Medicare program had covered influenza vaccination during the years noted, it would have incurred a net cost for each vaccination of \$13 per year of healthy life gained for medical costs connected with influenza and \$791 per year gained if costs of treating other illnesses in later life were included.

*Pneumococcal vaccine.* Cost-effectiveness of vaccination against pneumococcal pneumonia was examined by the Office of Technology Assessment, U.S. Congress.<sup>47</sup> The cost-effectiveness ratio, based on a single hypothetical vaccination program in 1978 and emphasizing a similar cost-effectiveness model as per Riddiough and colleagues,<sup>46</sup> was \$1,000 per year of healthy life gained. This is about six times as cost effective as giving pneumococcal vaccine to those 45-64 years of age.<sup>11</sup> The net cost is at the low (favorable) end of cost-effectiveness results (Table II). If the vaccination rate were assumed to be 21.5%, the net cost to society would be approximately 26 million dollars, which would add about 22,000 quality-adjusted life years.

TABLE II. COST-EFFECTIVENESS RATIO  
FOR VACCINATION AND OTHER PREVENTIVE SERVICES

<i>Service</i>	<i>Age of recipient</i>	<i>Net costs/year healthy life gained*</i>
Tetanus-diphtheria vaccination	> 65 yr. (nursing home resident/patient)	\$1,000,000 + <sup>45</sup>
Influenza vaccination	> 65 yr.	\$1,782 <sup>46</sup>
Pneumococcal vaccination	> 65 yr.	\$1,000 <sup>47</sup>
Hypertension screening	Adults	\$5,800-13,200 <sup>48</sup>
Pap smear	Women 30-39 yr.	\$16,000 <sup>48</sup>

\*Values are adjusted for disability days, including medical costs in extended years of life and discounted at 5% (except for Pap smear).

The estimated net cost to the Medicare program would be about \$5 per patient vaccinated, \$1,200 per quality life year gained, or a total net discounted cost of \$26 million.<sup>47</sup>

The Office of Technology and Assessment recently updated the 1978 analysis.<sup>49</sup> Certain important base-case assumptions were reevaluated, including the prevalence of pneumonia caused by *S. pneumoniae* (now assumed 10% versus 15%) and the duration of immunity (now assumed closer to three years versus eight years). Changes in these variables, plus updated information on cost of vaccination and medical costs in extended years of life, provide a new cost-effectiveness ratio expressed in 1983 costs. The estimated net costs of vaccination of an elderly person would be \$6,154 per health life year gained. The estimated net Medicare expenditures per vaccination would range from \$4,366 to \$8,345 per year of healthy life gained. Based on a vaccination rate of approximately 25%, Medicare would have spent between \$37 million and \$69 million to gain about 8,400 years of healthy life for its elderly beneficiaries.

#### UTILIZATION OF RECOMMENDED VACCINES

Although few data are available, there is no doubt that there is an unacceptably low utilization of vaccination for older persons. There are no published reports on the utilization of tetanus-diphtheria toxoid by older persons. The high case-rate in older persons and personal experience, however,

suggest that the vaccination rate is considerably less than the rates for influenza for pneumococcal vaccines and probably less than 5%. The Centers for Disease Control surveyed the use of influenza vaccines and found that only 20% of older people are immunized each year.<sup>50</sup> Data from manufacturers of pneumococcal vaccine suggest that approximately 11.1 million doses have been distributed (based on doses sold as opposed to doses used) in the United States from 1978 to 1983. If the target population for pneumococcal vaccine is the same group that is at risk for complications of influenza, this would include approximately 12 million high-risk older people with chronic diseases and an additional 13.5 million healthy older people. From these figures it is estimated that pneumococcal vaccine sales would have covered only about 35% of the high-risk and approximately 25% of the total elderly population.<sup>49</sup>

#### STRATEGIES TO IMPLEMENT CURRENT RECOMMENDATIONS

In 1979 The Surgeon General's Report on Health Promotion and Disease Prevention listed 18 immunization goals as "Objectives for the Nation."<sup>51</sup> Pertinent to this discussion were the objectives that by 1990 the reported incidence of tetanus should be reduced to fewer than 50 cases per year, and at least 60% of the high-risk population should have received influenza and pneumococcal vaccines. With the possible exception of the role of pneumococcal vaccine in nursing home settings, clearly current recommendations for immunization of older persons with tetanus-diphtheria toxoid and influenza and pneumococcal vaccines are appropriate. It is also clear that these diseases will not be prevented, and the objectives noted above will not be met by recommendations alone. Efforts to implement the current recommendations and meet these objectives will require that older people be immunized. This will demand new strategies that must focus on several important aspects.

*Identify persons with high-risk conditions.* In the case of tetanus this is probably best done by identifying all older people with soft tissue injuries as being at high risk for tetanus. Recent national and regional surveys document the major problem of inappropriate treatment (usually undertreatment) of patients with tetanus-prone wounds.<sup>3,52</sup> Routine immunization with the full primary series should be considered for those likely to be inadequately immunized or not immunized at all. Today this is primarily the elderly, especially elderly women. Routine single booster doses, after the initial series, must be given every 10 years regardless of the patient's age. After an

injury, a single booster should not be given to an older patient with an unknown immunization history. If the history is doubtful, the elderly patient should receive tetanus-diphtheria toxoid and passive immunization if the trauma is more than a clean minor wound. The primary immunization series should then be completed. In addition, promptly immunize, or give boosters as indicated, for debilitated people, including nursing home residents and patients with cutaneous ulcerations or vascular complications. The immunity status of older persons should be determined prior to elective surgery, especially surgery involving the gastrointestinal tract and adequate immunization provided.

Older patients with underlying chronic diseases, especially cardiac and respiratory conditions, comprise a substantial proportion of the American population and account for at least 50% of the hospitalizations and 75% to 80% of the deaths attributable to pneumonia and influenza.<sup>12</sup> These patients are easily identified because they have, by definition, required regular medical follow-ups in the community or required hospitalization or institutionalization in nursing homes during the preceeding year. Efforts to provide immunization of older people with influenza and pneumococcal vaccines should be promoted as noted below.

*Improve the delivery of vaccines.* The low incidence of tetanus in the United States among infants, children, and young adults is a result of widespread immunization programs supported by pediatricians, mandated programs for schools and military regulations. This leaves the older generation largely unprotected because there are no properly supported programs for them. Here more than anywhere else practicing physicians can take the lead in making sure that every patient that they see is immunized with tetanus-diphtheria toxoid to prevent this "inexcusable disease"

Physicians also need to become more involved in the prevention of influenza and pneumococcal pneumonia in older persons. Of the elderly, 80% receive immunization with influenza vaccines in private physicians' offices or clinics.<sup>54</sup> In all likelihood, the pattern of use for pneumococcal vaccine is similar.<sup>55</sup> The finding that almost two thirds of pneumococcal immunizations are given from September through November (the same season as recommended for influenza vaccine) despite no seasonal limitation for pneumococcal vaccine further emphasizes the important role of practicing physicians. New initiatives here might include direct payments to physicians for each dose administered to older patients with high-risk conditions. This might prove cheaper than large public programs in which acceptable rates are vari-

able and low. Physicians would also have an incentive to notify and to call in their high-risk patients, which would increase the acceptance rate.

To date, the general attitude of the public and physicians has focused on offering immunization for older patients in public clinics or physicians' offices, which is appropriate, especially for healthy older people. Although these sites will remain the principal setting for immunization against influenza and pneumococcal disease, hospital-based immunization programs can provide a major opportunity to improve the vaccination status of older persons.<sup>56,57</sup> If chronic care facilities are included, up to 85% of the pneumonia and influenza-associated deaths among high-risk older people occurred among those who received medical care during the previous year.<sup>12</sup> A recent study, however, documented that nursing homes that require written informed consent have influenza vaccination rates of approximately 60% versus vaccination rates of approximately 90% for those facilities that do not require this procedure.<sup>58</sup> If this is a general phenomenon in all nursing homes and/or if appropriate means of "informing" residents and their families are not developed, then nursing homes and other chronic care facilities will unfortunately not serve well as care settings to implement vaccine recommendations for older persons.

*Improve the acceptance of older persons.* If immunization rates are to be improved among older people, they themselves may have to become their own advocates. Although there is little information on tetanus-diphtheria toxoid, the lack of acceptance by older people of influenza and pneumococcal vaccines is frequently related to the lack of information and proper guidance by their physicians.<sup>54,59</sup> Furthermore, although physicians seem to know the importance and appropriateness of vaccines for older people,<sup>60,61</sup> they greatly underprescribe vaccines for their patients.

Perhaps efforts to change future preventive health behaviors of patients should be directed at the patients themselves. Previous studies have identified several reasons why the public does not seek vaccination.<sup>62</sup> These include personal readiness factors which identify personal attitudes that may affect a person's willingness to seek vaccination including: perceived personal susceptibility to a particular disease (includes perceived likelihood of local occurrence of the disease), perceived seriousness of the disease and perceived safety and efficacy of the vaccine. A second category, social and situational factors, includes social pressure and convenience of vaccination. Additional factors include vaccination costs and health insurance coverage.<sup>63</sup> Much information is needed to reevaluate these factors in the present social/economic climate.

Many older people have fears and doubts about the effectiveness and safety of vaccines and are amenable to suggestions from their physicians about future vaccinations.<sup>64</sup> Older patients and their families should receive full and accurate information concerning the efficacy and safety of the vaccination, and the relative risk of serious side-effects for people their age and with their health problems versus the relative risk and dangers to them of contracting the disease (or its complications) against which the vaccine is designed to protect them. This could be accomplished best by direct discussions with this high-risk group in special settings, e.g., nutrition and recreation centers, high rise apartments, church affairs, etc. Additional studies are needed to help vaccine promoters to assess the types of education and motivation needed for targeted persons to become immunized.<sup>65</sup>

*Establish mandatory immunization programs.* Although there is growing evidence of a new interest in the importance of vaccination for older people, much of this effort is related to restating already appropriate recommendations.<sup>1,2</sup> Even the efforts noted above have been tried before, although in a different social and economic climate and with fewer older persons at risk. Thus, it seems likely that bold new steps will be required if the objectives for 1990 are to be accomplished.

Failure to immunize adequate numbers of older people is a marked contrast to the success achieved with children since the National Childhood Immunization Initiative program was launched in 1977.<sup>65</sup> To promote childhood immunizations, most states and many local governments mandate selected vaccinations for school-aged children. Enforcement of such laws appears to raise vaccination rates in some areas.<sup>63</sup> For immunization such as influenza and pneumococcal vaccines and for tetanus-diphtheria toxoid for adults there are no such laws. Moreover, the current liability fears of both physicians and vaccine manufacturers will probably require that these vaccines remain strictly voluntary. Medicare specifically excludes payment for immunizations to prevent disease, and immunizations are not a service mandated by the federal government as a condition for state participation in the Medicaid program.<sup>63</sup> Thus, it is unlikely that federal or state mandated programs for immunization of older persons will be proposed in the near future.

Accreditation-supported immunization programs, however, might be feasible. State physician licensure requirements could, with some exceptions, include immunization of older persons as a standard of practice. In addition, the American Medical Association could identify and promote such a standard of practice. Hospital-based immunization programs could be "recom-

mended'' by the Joint Commission on the Accreditation of Hospitals and state accreditors. An approved influenza immunization program for residents or patients and personnel in nursing homes could be a requirement for state licensure. States could require such a program as part of nursing homes eligibility for Medicare reimbursement. The federal government jointly finances immunizations with those states that include vaccinations in their Medicaid benefit packages<sup>62</sup>.

#### SUMMARY

The above suggestions for implementing existing recommendations for immunization of older people may or may not be successful and, if successful, will require much time to develop and complete. Infectious disease specialists, however, can play a major role now. First, we can act as effective role models by implementing current recommendations in our own patients and make recommendations in those elderly patients that we see in consultation. This would be especially effective in promoting hospital-based immunization programs with house staff and primary physicians. Our critical role as educators for other physicians and, most important, for physicians in training as primary care physicians has already been emphasized.<sup>66</sup> Finally, as clinical investigators working with primary care physicians and other health-care team members, we can provide much needed information on the efficacy and safety of vaccines in older persons. These and other efforts will be necessary before the rates of immunization of older people improve.

#### REFERENCES

1. Committee on Immunization: *Guide for Adult Immunization*, 1st ed. Philadelphia: American College of Physicians, 1985, p. 132.
2. Centers for Disease Control: Adult immunization: recommendations of the Immunization Practices Advisory Committee (ACIP). *Morb. Mort. Weekly Rep.* 33:1S-68S, 1984.
3. Centers for Disease Control: Tetanus—United States, 1982-1984. *Morb. Mort. Weekly Rep.* 34:62-611, 1985.
4. Weiss, B.P., Strassburge, M.A., and Feeley, J.C.: Tetanus and diphtheria immunity in an elderly population in Los Angeles County. *Am. J. Public Health* 73:802-04, 1983.
5. Crossley, K., Irvine, P., Warren, J.B., et al.: Tetanus and diphtheria immunity in urban Minnesota adults. *J.A.M.A.* 242:2298-2300, 1979.
6. Ruben, F.L., Nagel, J., and Fireman, P.: Antitoxin responses in the elderly to tetanus-diphtheria (Td) immunization. *Am. J. Epidemiol.* 108:145-49, 1978.
7. Centers for Disease Control. Immunization Practices Advisory Committee (ACIP): Diphtheria, tetanus and pertussis: Guidelines for vaccine prophylaxis and other preventive measures. *Morb. Mort. Weekly Rep.* 34:405-26, 1985.
8. Solomonova, K. and Vizev, S.: Immunological reactivity of senescent and old people actively immunized with teta-



- nus toxoid. *Z. Immun.-Forsch. Bd.* 146:S.81-90, 1973.
9. Solomonova, K. and Vizev, S.: Secondary response to boosting by purified aluminum-hydroxide-adsorbed tetanus anatoxin in aging and in aged adults. *Immunobiology* 158:312-19, 1981.
  10. Centers for Disease Control: Adverse events following immunization. *Morb. Mort. Weekly Rep.* 34:43-47, 1985.
  11. Schoenbaum, S.C.: A Perspective on the Benefits, Costs and Risks of Immunization. In: *Seminars in Infectious Disease*, Weinstein, L. and Fields, B.N., editors. New York, Thieme-Stratton, 1980.
  12. Barker, W.H. and Mullooly, J.P.: Impact of epidemic type A influenza in a defined adult population. *Am. J. Epidemiol.* 112:789-813, 1980.
  13. Centers for Disease Control. Immunization Practices Advisory Committee (ACIP): Prevention and control of influenza. *Morb. Mort. Weekly Rep.* 35:317-31, 1986.
  14. Centers for Disease Control, Immunization Practices Advisory Committee (ACIP): Monovalent influenza A(H1N1) vaccine. *Morb. Mort. Weekly Rep.* 35:517-21, 1986-1987.
  15. Douglas, R.G., Jr., and Betts, R.F.: Influenza Virus. In: *Principles and Practice of Infectious Diseases*, Mandell, G.L., Douglas, R.G., Jr., and Bennett, J. E., editors. New York, Wiley, 1979, pp. 1135-67.
  16. Couch, R.B. and Kasel, J.A.: Immunity to influenza in man. *Ann. Rev. Microbiol.* 37:529-49, 1983.
  17. Bentley, D.W.: Immunization for the Elderly. In: *Medicine and Old Age: Immunology and Infection*, Fox, R.A., editor. London, Churchill Livingstone, 333-70, 1984.
  18. Arden, N.H., Patriarca, P.A., and Kendal, A.P.: Experiences in the Use and Efficacy of Inactivated Influenza Vaccine in Nursing Homes. In: *Options for the Control of Influenza*, Kendal, A.P. and Patriarca, P.A., editors. New York, Liss, 1986, pp. 155-60.
  19. Kluge, R.M. and Waldman, R.H.: Antibody to swine influenza virus in serum and nasal secretions of volunteers over the age of 55 years. *J. Infect. Dis.* 140:635-36, 1979.
  20. Stuart, W.H., Dull, H.B., Newton, L.H., et al.: Evaluation of monovalent influenza vaccine in a retirement community during the epidemic of 1965-1966. *J.A.M.A.* 209:232-38, 1969.
  21. Barker, W.H. and Mullooly, J.P.: Influenza vaccination of elderly persons. *J.A.M.A.* 244:2547-49, 1980.
  22. Patriarca, P.A., Weber, J.A., Parker, R.A., et al.: Efficacy of influenza vaccine in nursing homes: Reduction of illness and complications during an influenza A (H3N2) epidemic. *J.A.M.A.* 253:1136-39, 1985.
  23. Mathur, U., Bentley, D.W., Hall, C.B., et al.: Influenza A/Brazil/78(H1N1). Infection in the elderly. *Am. Rev. Respir. Dis.* 123:633-35, 1981.
  24. Mufson, M.A., Oley, G., and Hughey, D.: Pneumococcal disease in a medium-sized community in the United States. *J.A.M.A.* 248:1486-89, 1982.
  25. Patrick, K.M. and Woolley, F.R.: A cost-benefit analysis of immunization for pneumococcal pneumonia. *J.A.M.A.* 245:473-77, 1981.
  26. Filice, G.A., Darby, C.P., and Fraser, D.W.: Pneumococcal bacteremia in Charleston County, South Carolina. *Am. J. Epidemiol.* 112:828-35, 1980.
  27. Schwartz, J.S.: Pneumococcal vaccine: clinical efficacy and effectiveness. *Ann. Intern. Med.* 96:208-20, 1982.
  28. Fried, M.A.: Epidemiological Study of Pneumococcal Disease. Annual Contract Progress Report, NIAID, Contract No. NIAID 72-25130. San Francisco, Kaiser Permanente Medical Center, March 1, 1972-August 31, 1973.
  29. Bentley, D.W.: Pneumococcal vaccine in the institutionalized elderly: review of past and recent studies. *Rev. Infect. Dis.* (Suppl.):S61-70, 1981.
  30. Centers for Disease Control: Update: pneumococcal polysaccharide vaccine usage—United States. *Morb. Mort. Weekly Rep.* 33:273-73, 281, 1984.
  31. Austrian, R. and Gold, J.: Pneumococcal bacteremia with especial reference to bacteremic pneumococcal pneumonia. *Ann. Intern. Med.* 60:759-76, 1964.

32. Gabor, E.P. and Seeman, M.: Acute febrile systemic reaction to polyvalent pneumococcal vaccine. *J.A.M.A.* 242:2208-09, 1979.
33. Landesman, S.H. and Schiffman, G.: Assessment of the antibody response to pneumococcal polysaccharide vaccine in high-risk populations. *Rev. Infect. Dis.* 3:S184-96, 1981.
34. Mufson, M.A., Krause, H.E., and Schiffman, G.: Long-term persistence of antibody following immunization with pneumococcal polysaccharide vaccine. *Proc. Soc. Exp. Biol. Med.* 173:270-75, 1983.
35. Ammann, A.J., Schiffman, G., and Austrian, R.: The antibody responses to pneumococcal capsular polysaccharides in aged individuals. *Proc. Soc. Biol. Med.* 164:312-16, 1980.
36. Hilleman, M.R., Carlson, A.J., Jr., McLean, A.A., et al.: Streptococcus Pneumoniae polysaccharide vaccine: age and dose responses, safety, persistence of antibody, revaccination, and simultaneous administration of pneumococcal and influenza vaccines. *Rev. Infect. Dis. (Suppl.)* 3:531-42, 1981.
37. Hirschmann, J.V. and Lipsky, B.A.: Pneumococcal vaccine in the United States: a critical analysis. *J.A.M.A.* 246:1428-32, 1981.
38. Bolan, G., Broome, C.V., Facklam, R.R., et al.: Pneumococcal vaccine efficacy in selected populations in the United States. *Ann. Intern. Med.* 104:1-6, 1986.
39. Shapiro, E.D. and Clemens, J.D.: A controlled evaluation of the protective efficacy of pneumococcal vaccine for patients at high risk of serious pneumococcal infections. *Ann. Intern. Med.* 101:325-30, 1984.
40. Bentley, D.W., Iba, K., Mamot, K., et al.: Pneumococcal vaccine in the institutionalized elderly: design of a nonrandomized trial and preliminary results. *Rev. Infect. Dis. (Suppl.)*:S71-81, 1981.
41. Borgano, J.M., McLean, A.A., Vella, P.P., et al.: Vaccination and revaccination with polyvalent pneumococcal polysaccharide vaccines in adults and infants. *Proc. Soc. Exp. Biol. Med.* 157:148-54, 1978.
42. Williams, J.G. and Sanders, C.R.: Cost-effectiveness and cost-benefit analyses of vaccines. *J. Infect. Dis.* 144:486-93, 1981.
43. Sherman, F.T.: Tetanus and the institutionalized elderly. *J.A.M.A.* 244:2159, 1980.
44. Irvine, P. and Crossley, K.: Tetanus and the institutionalized elderly. *J.A.M.A.* 244:2159-60, 1980.
45. Berg, R.L.: Prevention: Can we Reduce the Demand for Long-Term Care? In: *The Impact of Technology on Long-Term Care*, Grana, J.M. and McCallum, D.B., editors. Ann Arbor, MI, Braun-Brumfield, 1986, pp. 65-100.
46. Riddiough, M.A., Sisk, J.E., and Bell, J.C.: Influenza vaccination: cost-effectiveness and public policy. *J.A.M.A.* 249:3189-95, 1983.
47. Willems, J.S., Sanders, C.R., Riddiough, M.A., et al.: Vaccination against pneumococcal pneumonia—Cost-effectiveness of vaccination against pneumococcal pneumonia. *N. Engl. J. Med.* 303:553-59, 1980.
48. Willems, J.S., Sanders, C.R., Riddiough, M.A., et al.: Cost-effectiveness of pneumococcal vaccine. *N. Engl. J. Med.* 304:116-17, 1981.
49. Sisk, J.E. and Riegelman, R.K.: Cost-effectiveness of vaccination against pneumococcal pneumonia: an update. *Ann. Intern. Med.* 104:79-86, 1986.
50. Centers for Disease Control: *United States Immunization Survey*. Atlanta, DHHS, 1984.
51. Public Health Service: *Healthy People: The Surgeon General's Report on Health Promotion and Disease Prevention*. DHEW Publication No. 79-55071. Washington, D.C., Govt. Print. Off., 1979.
52. Brand, D.A., Acampora, D., Gottlieb, L.D., et al.: Adequacy of antitetanus prophylaxis in six hospital emergency rooms. *N. Engl. J. Med.* 309:636-40, 1983.
53. Edsall, G.: The inexcusable disease. *J.A.M.A.* 235:62-63, 1976.
54. Ennis, F.A., Tully, M., Barry, D.W., et al.: In: *Influenza: Virus, Vaccine, and Strategy*, Selby, P., editor, New York, Academic, 1976, pp. 311-18.

55. Fedson, D.S.: Influenza and Pneumococcal Immunization. In: *Ger. Med. Annual 1986*, Ham, R.J., editor. Oradell, N.J., Medical Economics Books, 1986, pp. 62-78.
56. Fedson, D.S. and Kessler, H.A.: A hospital-based influenza immunization program 1977-78. *Am. J. Public Health* 73:442-45, 1983.
57. Fedson, D.S.: Improving the use of pneumococcal vaccine through a strategy of hospital-based immunization: A review of its rationale and implications. *J. Am. Geriatr. Soc.* 33:142-50, 1985.
58. Patriarca, P.A., Weber, J.A., Meissner, M.A., et al.: Use of influenza vaccine in nursing homes. *J. Am. Geriatr. Soc.* 33:463-66, 1985.
59. Pianko, L., Sherman, F., Rehr, H., et al.: Acceptance of pneumococcal vaccination by the community-residing elderly. *Gerontologist* 21 (special issue):43, 1981.
60. Berk, S.L., Verghese, A., Berk, M.L., et al.: Survey of physician acceptance of the pneumococcal vaccine. *South. Med. J.* 77:450-54, 1984.
61. Patriarca, P.A., Schlech, W.F., Himan, A.R., et al.: Pneumococcal vaccination practices among private physicians. *Public Health Rep.* 97:406-408, 1982.
62. Rosenstock, I.M., Derryberry, M., and Carriger, B.K.: Why people fail to seek poliomyelitis vaccination. *Public Health Rep.* 74:98-103, 1959.
63. Riddiough, M.A., Willems, J.A., Saunders, C.R., et al: Factors affecting the use of vaccines: Considerations for immunization program planners. *Public Health Rep.* 96:535, 1981.
64. Aho, W.R.: Participation of senior citizens in the swine flu inoculation program: An analysis of health belief model variables in preventive health behavior. *J. Gerontol.* 34:201-08, 1979.
65. Hinman, A.R. and Jordan, W.S., Jr.: Progress toward achieving the 1990 immunization objectives. *Public Health Rep.* 98:436-43, 1983.
66. Eickhoff, T.C.: Immunization—an adult thing to do. *J. Infect. Dis.* 152:1-3, 1985.